RESPONSE UNDER 37 C.F.R. § 1.116
EXPEDITED PROCEDURE – Art Unit 1653
Attorney Docket Number 54763.8001.US02

RESPONSE

Interview Summary

On June 27, 2003, an interview was held between the undersigned, Examiner Low and Examiner Caputa. At the interview the Final Office Action was discussed, and in particular, the effective filing date of Roth et al.'s U.S. Patent No. 5,747,469 ("'469 Patent") and Zhang et al.'s U.S. Patent No. 6,069,134 ("'134 Patent") as 102(e) references and the showing required by Applicants to provoke an interference – 608(a) vs. 608(b).

Rejection of Claims under 35 U.S.C. §102(e)

The Office Action maintains the rejection of claims 1, 2, 4, 5, 8-15, 17-20 and 23 under 35 U.S.C. §102(e) as being anticipated by '469 and '134 Patents. Because the present application was filed prior to November 29, 2000 and has not been voluntarily published, the former version of 35 U.S.C. §102(e) applies:

> "A person shall be entitled to a patent unless...
> (e) the invention was **described** in a patent granted on an application for patent by another filed in the United States **before the invention thereof** by the applicant for patent..." (Emphasis added)

The effective date of a 102(e) reference which claims the same invention as a pending application is the earliest date filing date of an application that describes and enables the claimed invention. *In re Wertheim*, 646 F.2d 527, 209 USPQ 554 (CCPA 1981). At issue here, is whether the '469 and '134 Patents are entitled to the benefit of the filing date of the U.S. Patent Application Serial

No. 08/145,826, filed October 29, 1993, now U.S. Patent No. 6,410,010 ("'010 Patent"). If they are entitled to benefit, then Applicants must prepare a 608(b) showing to provoke an interference. If the '469 and '134 Patents are not entitled to benefit, then the 102(e) effective filing date is April 25, 1994 and Applicants would proceed under 608(a) since the parties' respective filing dates are less than three months apart .

To demonstrate that the '469 and '134 Patents are not entitled to the benefit of the filing date of '010 Patent's filing date, Applicants address the support in the specification of the '010 Patent for the claims of the '469 and '134 Patents. The independent claims of the '469 and '134 Patents are set forth below. If the independent claims are not supported by the earlier filed application, then the narrower dependent claims cannot be supported as they add additional limitations.

The '469 Patent has 105 claims; claims 1 and 51, set forth below, are the only independent claims:

> "1. A method of killing a tumor cell in a patient in need thereof, comprising directly administering to said tumor cell therapeutically effective amounts of a viral vector and a DNA damaging agent, wherein said viral vector comprises a DNA sequence encoding p53 operatively linked to a promoter, and wherein expression of said p53 and DNA damage results in the killing of said tumor cell.
>
> 51. A method of treating cancer in a cancer patient, comprising directly administering to a tumor site therapeutically effective amounts of a viral vector and a DNA damaging agent, wherein said viral vector comprises a DNA sequence encoding p53 operatively linked to a promoter, and wherein expression of said p53 and DNA damage result in treatment of said cancer.

The '134 Patent has 69 claims, claims 1 and 3, set forth below, are the only independent claims.

> 1. A method of killing a tumor cell in a tumor of a human cancer patient, the method comprising the steps of:
>
> (a) introducing into said tumor an effective amount of polynucleotides encoding a functionally active p53;
>
> (b) expressing said p53 in said tumor cell, thereby enhancing the sensitivity of said tumor cell expressing said p53 to a first DNA damaging agent, and
>
> (c) contacting said tumor cell with said first DNA damaging agent, thereby killing said tumor cell.
>
> 3. A method for killing a tumor cell in a tumor of a human cancer patient, the method comprising the steps of:
>
> (a) contacting said tumor with a first DNA damaging agent;
>
> (b) introducing into said tumor an effective amount of polynucleotides encoding a functionally active p53; and
>
> (c) expressing p53 in said tumor cell, thereby enhancing the sensitivity of said tumor cell expressing p53 to said first DNA damaging agent, and wherein the expression of said p53 and DNA damaging agent result in the killing of said tumor cell.

In Applicants' prior response, Applicants explained that Applicants' pending claims and the claims of the '469 and '134 Patents all require a combination p53/cancer therapy – namely the delivering and expressing p53 gene in a tumor cell and exposing the tumor cell to "cancer therapy" or a "DNA damaging agent," both of these terms are defined in their respective specifications to mean chemotherapy, radiotherapy, etc. In the prior response Applicants (pp. 11, 16-18) also explained that the '010 Patent (the parent

specification at issue regarding benefit) did not describe and enable a combination p53/cancer therapy as claimed in the '469 and '134 Patents.

The Final Office Action addresses Applicants' position at page 5:

> The response comments regarding the Zhang *et al.* are unpersuasive because (column 2, line 60+) indicates providing efficient means to restore p53 functions by (column 3, line 25+) introducing wild type p53 genes into target cells (obviously the wild type gene encodes the wild type p53) and is unexpectedly effective in inhibiting the growth of cancer cells (column 3, line 38+) with astonishing efficiency (column 3, line 40-45). See also column 5, line 15+) and would not prelude the patient from receiving other palliative therapy (column 16, line 57+).

The disclosure in the '010 Patent that introduction of the wild type p53 gene into target cells inhibited the growth tumor cells was not "unexpected" (see '010 Patent, column 2, line 19-30) as it was a known tumor suppressor. What was unexpected was the effectiveness of the adenoviral vector for delivering the gene and the level of growth inhibition. '010 Patent, column 3, lines 34-45. That is in fact, the focus of the '010 Patent specification and claims – the adenoviral vector for p53 gene delivery. The only disclosure that the Office Action cites as support for a combination p53/cancer therapy is the following statement:

> Patients failing brachytherapy would also be eligible to receive gene therapy. Tumor can be removed from the airway with the laser of biopsy forceps. This can be done in conjunction with injection of the adenoviral constructs thus decreasing the volume that must be injected. The administration of the viral constructs would not preclude the patient from receiving other palliative therapy if the tumor progresses.

'010 Patent, column 16, line 53-60.

The above disclosure does not describe and enable a method of killing tumor cells by the combination of administering a p53 gene and a "DNA damaging agent", such as chemotherapy or radiotherapy, to a tumor cell as required by the claims of the '469 and '134 Patents. Further, the above disclosure teaches away from the combination p53/cancer therapy. Although the disclosure does not exclude other palliative therapies as noted by the Office Action, according to the disclosure, those palliative therapies should be used **"if the tumor progresses."** In other words, the '010 Patent teaches that when the p53 therapy fails to stop tumor progression, one could then try chemotherapy.

In marked contrast, the Applicants' invention "features a new method for enhancing the effect of a cancer therapy by introducing into tumor cells a source of wild-type therapy-sensitizing gene activity [p53] before subjecting the tumor cells to therapy." U.S. Patent Application Serial No. 09/335,461 ("'461 Application") p. 13, lines 35-38.

This combination p53/cancer therapy is more effective than either expression of wild-type p53 alone or cancer therapy alone.

> The method of combining p53 sensitization therapy with other therapy is more effective than either therapy alone. When exogenous wild-type p53 activity is introduced into a tumor cell, lower doses of drugs or radiation are needed to kill the cell, and the therapeutic window of concentrations over which drugs or radiation are needed to kill the cell, and the therapeutic window of concentrations over which drugs or radiation can be administered without toxicity is increased. In contrast to p53 gene therapy alone, which requires sustained p53 gene expression for tumor suppression, the combined effect of p53 sensitization therapy with other treatments requires only transient existence of a therapy – sensitizing portion of a wild-type p53 protein in the tumor cell during the treatment period to kill the tumor cell.

'461 Application, p. 14, lines 21-33.

This conclusion is further supported by the data shown in Figures 1 and 2 of the '461 Application which demonstrates the p53 transfected tumor cells are more susceptible to killing with chemotherapy (cisplatin, Figure 1) and radiotherapy (Figure 2). Further evidence supporting this conclusion is the Gjerset Declaration at ¶44 and Exhibit B.

Similar experiments disclosed in the '469 and '134 Patents show that the combination therapy of p53 and cisplatin is more effective than p53 alone or cisplatin alone in killing tumor cells. See Example 7 "Synergism Between p53 and DNA Damage" ('469 and '134 Patents at column 28) and Figures 12-13.

For all of the above reasons, Applicants respectfully request that the final rejection be withdrawn, the prosecution suspended and the application forwarded to the Board for a declaration of interference.

Respectfully submitted,
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Dated: July 25, 2003

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